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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,426	11/13/2001	Helle Woldike	5565.214-US	3262

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/30/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/044,426	WOLDIKE ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5 and 7-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This office action is in response to a request for continued examination, filed 5/14/03. Claims 1, 4, 5 and 7-10 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 7-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Barr et al. US 5,986,079, see entire document.

Barr et al. teach a method for producing Factor VII (e.g. column 10,line 66- column 11,line 12) in which mammalian cells express PACE and a precursor polypeptide DNA cleavable by PACE. These are encoded on the same or different plasmids (e.g. column 12, line 1-15). Mammalian cell lines contemplated for use in the invention include BHK, CHO and 293 cells (column 14, line 7-28). Serum-free medium is used for the expression of PACE in CHO cells (see e.g. example 5, column 32, line 5-20). Barr et al. teach that PACE (furin) was isolated based upon structural homology with Kex2 (e.g. column 3, line 47-63). PACE is a subtilisin-like endoprotease that cleaves at basic residues of a polypeptide e.g. Lys-Arg, Arg-Arg or Lys-Lys, is stimulated by calcium ions (column 6, line 1-13), and has a molecular weight of 86.7 kD (column 27,line 18). Given that the specification lacks a clear definition or description of a

variant, it is expected that the following definition from the Oxford online dictionary is appropriate- Variant, noun [C] something that differs slightly from other similar things. In this case, PACE can be reasonably considered a variant of Kex2.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5 and 7-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants recite a method for producing Factor VII comprising a DNA sequence encoding Kex2 variant having Kex2 enzymatic activity. Therefore, applicants claim a genus of endoproteases that have Kex2 activity.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. The claims recite a

method of producing Factor VII featuring the use of a DNA sequence encoding a Kex2 variant having Kex2 enzymatic activity. Several properties of Kex2 are disclosed 1) that it cleaves C-terminal to a Lys-Arg or Arg-Arg or Pro-Arg sequence 2) that it is present in a membrane fraction and requires calcium and 3) that it is a glycoprotein with molecular weight of 100-120 K Daltons (page 1 paragraph 0011. Applicant has disclosed that preferred yeast endoproteases for use in the invention are Kex2 and may be C-terminal truncations deprived of the transmembrane region or may contain an ER retention signal at the C-terminus. Neither applicant not the prior art provide a correlation between the structure of the recited variant and its activity. Relevant identifying characteristics of Kex2 variants are not disclosed in the specification. Given the diversity of variants, the lack of clear depiction of these variants in the specification and the inability to determine which variants will also contain the essential element of the invention, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of Kex2 with C-terminal truncations or an ER retention signal at the C-terminus species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-5 and 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "said endoprotease" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitation "the method" of claim 3. There is insufficient antecedent basis for this limitation in the claim as claim 3 has been cancelled. It would be remedial to recite "the method of claim 1".

Response to Arguments

Applicants traverse the rejection under 35 USC 112, first paragraph, by referring to the arguments on pages 2-3 of the amendment filed March 3, 2003, Paper No. 13, Applicant argues that the invention is the intracellular cleavage of Factor VII by a recombinantly co-expressed protein having Kex2 enzymatic activity. Therefore, while the applicants are not claiming proteins that have Kex2 activity, they are claiming the combination of Kex2 activity and nascent Factor VII. In this amendment, applicants state that a Kex2 variant is a protein having a sequence derived from that of wild-type Kex2 and closely enough related to the wild-type sequence that Kex2 enzymatic activity is retained.

Applicant's arguments filed 5/14/03 have been fully considered but they are not persuasive. Amendment of the claim language from a yeast derived endoprotease having Kex 2 enzymatic activtiy to a Kex 2 variant having Kex 2 enymatic activity adds the limitation that the endoprotease be a Kex2 variant which finds no clear basis in the original disclosure. The specification does not define or describe a Kex2 variant the scope of which is unclear. Neither the prior art nor the specification has provided adequate written description to support or illustrate the genus encompassed by the claim. Without knowing what the proteins are or what

they look like, there is no description of the method as broadly claimed. Furthermore, the applicant must convey with reasonable clarity to those skilled in the art that they were in possession of the invention. While the claims are not drawn to the Kex2 variants but to a method of producing Factor VII, that method requires use of a Kex2 variant. Therefore, Kex2 variants are a critical element of the recited methods and must be adequately described in order for the claimed methods to be adequately described. For the reasons outlined above, this is not the case.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3291.

Maria B Marvich, PhD
Examiner
Art Unit 1636

Donald R. Prouty
PATENT EXAMINER

MM
July 28, 2003